

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

**THIS PAGE BLANK (USPTO)**

---

# (12) UK Patent Application (19) GB (11) 2 283 173 (13) A

(43) Date of A Publication 03.05.1995

(21) Application No 9411992.2

(22) Date of Filing 15.06.1994

(30) Priority Data

(31) 05270970	(32) 28.10.1993	(33) JP
05270971	28.10.1993	
05270972	28.10.1993	

(71) Applicant(s)

Sansho Seiyaku Co Ltd

(Incorporated in Japan)

26-7 Oike 2-Chome, Ohnojo-shi, Fujioka 816, Japan

(72) Inventor(s)

Shinsuke Honda

(74) Agent and/or Address for Service

Marks & Clerk

57-60 Lincoln's Inn Fields, LONDON, WC2A 3LS,  
United Kingdom

(51) INT CL<sup>5</sup>

A61K 7/40 7/48 31/35 47/00 47/10 47/34 47/44

(52) UK CL (Edition N)

A5B BFE BFH BJB B160 B161 B170 B23X B23Y B23O  
B26Y B27Y B273 B275 B28Y B285 B30X B30Y B301  
B31Y B316 B34Y B340 B343 B35Y B351 B353 B36Y  
B362 B364 B40Y B401 B402 B406 B44Y B442 B443  
B446 B48Y B481 B482 B483 B485 B486 B50Y B502  
B503 B54Y B540 B541 B56Y B565 B566 B58Y B586  
B64Y B644 B822 B825 B826 B832 B841  
U1S S1310 S1330 S1342 S1343 S2416 S3012

(56) Documents Cited

JP 060048935 A JP 050078383 A JP 020200622 A  
US 4985455 A

(58) Field of Search

UK CL (Edition M) A5B BFE BFH BJB  
INT CL<sup>5</sup> A61K 7/40 7/42 7/48 31/35 47/00  
ONLINE DATABASES: WPI, CLAIMS, DIALOG/PHARM

(54) Epidermal composition comprising kojic acid and an ultra-violet light absorbent

(57) Epidermal composition comprises:

- (i) kojic acid (5-hydroxy-2-hydroxymethyl-gamma-pyrone) or a derivative (especially a glycoside) thereof;
- (ii) an ultra-violet light absorbent;
- (iii) at least one of:

- (A) fatty acid esters (including esters of polyhydric alcohols and sugars);
- (B) fatty acid glycerides;
- (C) hydrocarbons;
- (D) lipids (especially glycerophospholipids, sphingophospholipids or sphingoglycolipids);
- (E) fats or oils;
- (F) alcohols (including polyhydric alcohols and the alkyl ethers thereof, and sugar alcohols);
- (G) polyphenols (especially catechin, esters of gallic acid, flavone or tannin).

GB 2 283 173 A

PREPARATION FOR EPIDERMIS

This invention relates to a preparation for epidermis containing kojic acid and/or its derivative and an ultraviolet light absorbent, which further contains at least one member selected from the group consisting of fatty acid esters and fatty acid glycerides hydrocarbons, lipids and hardened or non-hardened fats and oils alcohols and polyphenols for improving stability and attaining lasting effectiveness of the kojic acid and/or its derivative.

As typical forms of preparation for epidermis, there are illustrated O/W (oil-in-water) emulsions and W/O (water-in-oil) emulsions, which are different from each other in water-to-oil composition ratio and physical properties but are both homogeneous preparations wherein oil phase or aqueous phase are stably emulsified and dispersed with the aid of a surfactant.

Kojic acid and its derivatives are known as useful agents having various excellent properties, as disclosed in Japanese Unexamined Patent Publication No. 55-157509, Japanese Examined Patent Publication No. S56-18569, S58-22151, S58-22152, S58-34446, S60-7961, S60-9722 and S60-10005, Japanese Unexamined Patent Publication No. S60-137253, Japanese Examined Patent Publication No. S61-10447 and S61-60801, Japanese Unexamined Patent Publication No. S62-5909, Japanese Examined Patent Publication No. S62-3820 and S63-27322, Japanese Unexamined Patent Publication No. H1-132502 and Japanese Examined Patent Publication No. H5-30422.

However, kojic acid and its derivatives (hereinafter these being in some cases merely referred

to as "kojic acids") are also known as agents which themselves have difficulty in acquiring stability. Particularly when the kojic acids are incorporated in the aforementioned O/W emulsion or W/O emulsion, it requires a highly sophisticated technique to design a proper formulation. Hence, there has been a pressing need for a technique which provides the kojic acids-containing preparation with enough stability to stand severe distributive machinery without giving unpleasant feeling upon application thereof to skin.

In the case of compounding the kojic acids in various preparations for the epidermis, they are likely to be exposed to ultraviolet light to varying degrees which can be an external cause of their discoloration or decomposition. Thus, it has been the practice to compound an ultraviolet light absorbent in a proper amount to depress damage by irradiation with ultraviolet light.

Examples thereof are illustrated in, for example, Japanese Unexamined Patent Publication No. S62-108804 and S64-83008 and Japanese Examined Patent Publication No. H4-46924.

Many of such ultraviolet light absorbents have a problem with solubility and separate out in the preparation, and fail to fully exhibit their ultraviolet light-absorbing ability, leading to a deteriorated stability of kojic acid.

In order to overcome this defect, solubilizing agents have properly been used. However, the use of oily solubilizing agent in a large amount causes a problem of giving an unpleasant feeling such as sticking feeling upon application to skin.

In addition, nonionic surfactants, which are properly used as surfactants upon forming a preparation containing kojic acids for external application in view of depressing coloration, giving a pleasant feeling upon application and being harmless to skin, have weaker emulsifying power in comparison with ionic surfactants and suffer decrease in emulsifying power in the presence of a highly polar ingredient or by the influence of pH level. Therefore, in the kojic acid-containing preparation which is usually adjusted to 4 to 5 in pH, incorporation of a highly polar ultraviolet light absorbent causes the problem of deteriorating emulsion stability with time.

It is, therefore, an object of the present invention to provide a preparation for epidermis which solves the above-described problems with the conventional kojic acid-containing preparation, i. e., which does not suffer separation of the ultraviolet light absorbent and has improved stability with time to coloration and decomposition of kojic acid and has an improved lasting effectiveness of the ingredient, and which is formed by adding at least one member selected from the group consisting of fatty acid esters and fatty acid glycerides, hydrocarbons, lipids and hardened or non-hardened fats and oils, alcohols and polyphenols to a preparation for external application containing kojic acid and/or its derivative.

Other objects, features and advantages of the present invention will become apparent from the detailed description of the preferred embodiments of the invention to follow.

As the kojic acid (5-hydroxy-2-

hydroxymethyl- $\gamma$ -pyrrone) to be used in the present invention as a first ingredient, a pure product of 5-hydroxy-2-hydroxymethyl- $\gamma$ -pyrrone, a fermentation liquor containing kojic acid as a major component obtained by cultivating a known bacterium strain capable of yielding kojic acid; a concentrate of the fermentation liquor; a product obtained by extracting kojic acid from the fermentation liquor and crystallizing the extract; and the like.

As the kojic acid derivatives, those which are disclosed in, for example, Japanese Examined Patent Publication No. S60-10005, H1-45472 and H3-74229, and esterified products of kojic acid and kojic acid derivatives wherein sugars are bound to the  $-\text{CH}_2\text{OH}$  group at 2-position of kojic acid disclosed in, for example, Japanese Examined Patent Publication No. S58-22151 and S58-22152 may be used alone or in combination of two or more.

The kojic acid and/or its derivative is compounded in the preparation in an amount of 0.001 to 10 % by weight, preferably 0.1 to 5 % by weight, based on the total amount of the preparation for external application.

The ultraviolet light absorbents to be used in the present invention as a second ingredient are not particularly limited. Preferred examples thereof include benzophenone derivatives such as oxybenzone, oxybenzonesulfonic acid, sodium hydroxymethoxybenzophenonesulfonate and dihydroxydimethoxybenzophenone; salicylic acid derivatives such as ethylene glycol salicylate, homomenthyl salicylate and phenyl salicylate; urocanic acid and ethyl urocanate; cinnamic acid derivatives such as 2-ethylhexyl p-methoxycinnamate and octyl methoxycinnamate;

p-aminobenzoic acid derivatives such as glyceryl p-aminobenzoate and 2-ethylhexyl p-dimethylaminobenzoate; dibenzoylmethane derivatives such as 4-tert-butyl-4'-methoxydibenzoylmethane; and benzotriazole derivatives such as 2-(2-hydroxy-5-methylphenyl)-benzotriazole. These compounds may be used alone or in combination of two or more. In addition, other known animal or vegetable extracts having ultraviolet light-absorbing ability may properly be used alone or in combination.

Amounts of these ultraviolet light absorbents are somewhat varied depending upon the kind thereof but, usually, they are used in an amount of 0.001 to 10 % by weight, preferably 0.1 to 5 % by weight, based on the total amount of the preparation for external application.

As the fatty acid esters to be used in the present invention as a third ingredient, there are illustrated higher alcohol fatty acid esters such as isopropyl adipate, avocado oil fatty acid ethyl ester, isocetyl isostearate, isopropyl isostearate, isodecyl isononanoate, octyl isopalmate, octyl isopelargonate, octyldodecyl erucate, octyl hydroxystearate, octyldodecyl oleate, oleyl oleate, decyl oleate, dioctyl succinate, hexyldecyl dimethyloctanoate, isocetyl stearate, butyl stearate, octyldodecyl lactate, oleyl lactate, cetyl lactate, myristyl lactate, lauryl lactate, isostearyl palmitate, isopropyl palmitate, octyl palmitate, cetyl palmitate, castor oil fatty acid methyl ester, diethyl phthalate, eicosanyl propionate, stearyl heptanoate, isostearyl myristate, isocetyl myristate, isotridecyl myristate, isopropyl myristate, octyldodecyl myristate, cetyl myristate, decyl myristate, butyl myristate, myristyl myristate, hexyl laurate, octyldodecyl ricinoleate, cetyl ricinoleate, isopropyl linolate and diisostearyl malate; ethylene glycol fatty acid esters such as ethylene glycol



fatty acid ester, ethylene glycol dioctanoate, ethylene glycol dioleate, ethylene glycol distearate and ethylene glycol monostearate; polyethylene glycol fatty acid esters such as diethylene glycol laurate, diethylene glycol dilaurate, polyoxy 40 stearate, polyethylene glycol palmitate, polyoxyethylene coconut oil fatty acid ester (6E.O.), polyethylene glycol myristate, polyethylene glycol monooleate and polyethylene glycol monolaurate; propylene glycol fatty acid esters such as propylene glycol fatty acid ester, self-emulsifiable propylene glycol stearate, propylene glycol monostearate, propylene glycol dioleate, propylene glycol dicaprylate and propylene glycol dicaprylate; glycol fatty acid esters such as neopentylglycol dioctanoate, neopentylglycol dicaprylate, butanediol dimontanate and alkylene (18, 20) straight chain glycol monoisostearate; trimethylolpropane fatty acid esters such as trimethylolpropane triisostearate and trimethylolpropane trioctanoate; pentaerythritol fatty acid esters such as pentaerythritol fatty acid (1), pentaerythritol tetraoctanoate and pentaerythritol tetramyristate; sorbitol fatty acid esters such as sorbitol sesquiisostearate, sorbitol sesquioleate, sorbitol trioleate and sorbitol coconut oil fatty acid ester; polyoxyethylene sorbitol fatty acid esters such as polyoxyethylene sorbitol (20E.O.) isostearate, polyoxyethylene sorbitol (20E.O.) trioleate, polyoxyethylene sorbitol (20E.O.) tristearate, polyoxyethylene sorbitol hexastearate, polyoxyethylene sorbitol bees wax, polyoxyethylene coconut oil fatty acid sorbitol ester (20E.O.) and polyoxyethylene sorbitol (6E.O.) monooleate; and sugar fatty acid esters such as sucrose benzoate, sucrose acetate isobutyrate, sucrose stearate and sucrose ester of coconut oil fatty acid and, as the fatty acid glycerides, there are illustrated glycerol fatty acid esters such as glyceryl arachate, glyceryl isostearate, glyceryl oleate (1), wheat germ oil

fatty acid glyceride, mixed fatty acid triglyceride, isopalmitic acid diglyceride, hydrogenated soybean oil fatty acid diglyceride, myristic acid diglyceride, cotton seed fatty acid diglyceride, coconut oil fatty acid diglyceride, hydrogenated soybean oil fatty acid diglyceride, glyceryl stearate malate, sesquioleic acid glyceride, capric and caprylic acid triglyceride, tallow fatty acid triglyceride, myristic acid triglyceride, coconut oil fatty acid triglyceride, saturated fatty acid triglyceride and saturated fatty acid glyceride (2), polyglycerol fatty acid esters such as diglyceryl isostearate, diglyceryl oleate, diglyceryl stearate, diglyceryl diisostearate, tetraglyceryl oleate, tetraglyceryl laurate, hexaglyceryl oleate, hexaglyceryl laurate, decaglyceryl laurate, decaglyceryl diisostearate and decaglyceryl decaoleate; and polyoxyethylene glycerol fatty acid esters such as polyoxy-ethylene glyceryl isostearate, polyoxyethylene glyceryl triiso-stearate, polyoxyethylene glyceryl oleate and polyoxyethylene glyceryl monostearate. Of these, middle-chain fatty acid (containing 6 to 12 carbon atoms) monoglycerides, diglycerides and triglycerides are most preferred. These compounds may be used alone or in combination of two or more.

As the hydrocarbons to be used in the present invention as a third ingredient, there are illustrated paraffinic hydrocarbons and olefinic hydrocarbons such as ,X -olefin oligomers, liquid isoparaffin, plastibase (product of Nippon Squib), polyisobutylene and polybutene, with those containing 10 or more carbons and having a lower polarity being preferably used.

As the lipids, phospholipids are most preferred, and examples thereof include glycerophospholipids such as phosphatidyl choline, phosphatidyl inositol,

phosphatidylethanolamine and phosphatidyl serine obtained by extraction from natural products such as egg yolk, soybean and corn; sphingophospholipids such as sphingomyelin and ceramide ciliatin; synthetic phospholipids such as sphingoglycolipid, distearoylphosphatidyl choline and dipalmitoylphosphatidyl choline; etc.

As the hardened or non-hardened fats and oils, there are illustrated, as preferred examples, completely hardened castor oils having a polymerization degree of about 40 to about 100 such as polyoxyethylene hardened castor oil, triisostearic acid polyoxyethylene hardened castor oil, isostearic acid polyoxyethylene hardened castor oil, lauric acid polyoxyethylene hardened castor oil, polyoxyethylene castor oil and polyoxyethylenesorbitol bees wax. These may be used alone or in combination. As the alcohols to be used in the present invention as a third ingredient, lower alcohols such as ethanol, propanol and isopropanol; higher alcohols such as octyldodecanol, olive oil alcohol, oleyl alcohol, stearyl alcohol, cetostearyl alcohol, decyltetradecanol, hexyldecanol, jojoba alcohol, myristyl alcohol and lauryl alcohol; polyhydric alcohols such as alkylene (containing 15 to 18 carbon atoms) glycol, alkylene (containing 20 to 30 carbon atoms) glycol, ethylene glycol, highly polymerized polyethylene glycol, diglycerin, dipropylene glycol, hexylene glycol, polyethylene glycol 200, polyethylene glycol 300, polyethylene glycol 400, polyethylene glycol 600, polyethylene glycol 1000, polyethylene glycol 1500, polyethylene glycol 4000, polyethylene glycol 6000, polyethylene glycol 20000, polypropylene glycol 400 and polypropylene glycol 1200; sugaralcohols such as fruit sugar, xylitol, D-xylene, sorbitol, D-sorbitol, glucose, multitol, maltose, D-mannitol and amylolytic sugaralcohol; and polyhydric

alcohol alkyl ethers such as isostearyl glyceryl ether, ethylene glycol ethyl ether, ethylene glycol methyl ether, ethylene glycol monobutyl ether, chimyl alcohol, diethylene glycol ethyl ether, diglyceryl oleyl ether and batyl alcohol are illustrated as preferable examples.

As the polyphenols, pyrogallol; phloroglucinol; catechins such as catechin, epicatechin, gallocatechin, catechin gallate, gallocatechin gallate, epicatechin gallate, epigallocatechin gallate and epigallocatechin; glucogallin; proanthocyanidin; gallic acid; gallic acid esters such as propyl gallate, isoamyl octyl gallate and dodecyl gallate; flavones such as rutin, quercetin, quercetagen, quercetagenin and gossypetin penta-O-galloyl glucose; tannic acid; various tannins such as gallotannin, ellagitannin and condensed tannins extracted from ast--ingent Japanese persimmon or tea; and shikimic acid are illustrated as preferable examples, which may be used alone or in combination of two or more.

Amounts of the third ingredient somewhat varies depending upon the kind thereof but, usually, they are added in an amount of 0.001 to 20 % by weight, preferably 0.1 to 10 % by weight, based on the total amount of the preparation.

The above-described first to three ingredients may be formed into a preparation for external application in a known manner. Such preparation does not suffer separation of the ultraviolet light absorbent, thus being a stable emulsion preparation having good stability with time, in which the kojic acids show improved stability to coloration and decomposition with time and exhibit lasting effectiveness.

Needless to say, form of the preparation of the

present invention is not limited to the emulsion type such as O/W emulsion and W/O emulsion, but may be a transparent type by properly selecting the ingredients. In addition, the present invention may also be applicable as a fundamental technique for forming multi-layer emulsion preparations such as W/O/W or O/W/O emulsions or microcapsule preparations.

The preparation of the present invention for the epidermis is not particularly limited as to application form, and may be widely used in a known application form of medicines, quasi-drugs and cosmetics such as cataplasma, plaster, paste, cream, ointment, aerosol, emulsion, lotion, essence, pack, gel, powder, foundation, suncare, bath salts, and the like.

In forming the preparation of the present invention, various known and conventionally used effective ingredients may optionally be incorporated as the case demands in amounts not spoiling the objects of the present invention. Examples of such known effective ingredients include capillary vasodilators such as carpronium chloride, cepharanthine, vitamin E, vitamin E nicotinate, nicotinic acid, nicotinic acid amide, benzyl nicotinate, ginger tincture and chili tincture; coolers such as camphor, mentol and peppermint oil; antimicrobial agents such as hinokitiol, benzalkonium chloride and undecylenic acid; anti-inflammatory agents such as adrenal cortical hormone, aminocaproic acid, lysozyme chloride, glycyrrhizin and allantoin; fairness-imparting agents such as ascorbic acid and arbutin; various extracts of animal or vegetable origin such as placenta extract, liver extract, lithospermum root extract and extract of culture liquor of lactic acid bacteria.

In addition to the known effective ingredients,

various known additives such as humectants, antiseptics, antioxidants, chelating agents, pH-adjusting agents, perfumes and colorants may also be used, as well as a base ingredient such as a fat and oil, within a range of not spoiling the objects of the present invention in the above-described application forms of medicines, quasi-drugs and cosmetics.

The present invention is now described in more detail by reference to experiments and formulations which, however, are not construed to be limitative at all.

#### Experiment 1

##### Preparation stability test

##### Method of experiment:

Various creams (pH: about 4.5) were prepared according to the formulations shown in Table 1. After placing them in ml (4-ounce) candle bottle, they were stored for 2 months under the severe condition of 50°C while irradiating with ultraviolet light. After 2 months, color difference ( $\Delta E$ ) was measured (using a color-difference meter, Z-1001DP, made by Nihon Denshoku Kogyo). In this occasion, observation of change in appearance (separation of the ultraviolet light absorbent and stability of the emulsion) and evaluation of application feeling were also conducted.

##### Results of the experiment:

As is shown in Table 1, the preparations in accordance with the present invention containing ingredients 1 to 8 suffered no separation of the ultraviolet light absorbent and showed an extremely good emulsion stability. Coloration of kojic acid contained in the preparations was not observed, and application feeling was kept good.

Table 1-1

[illegible]

(contd.)

18. Natural vitamin E	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
19. Polyoxyethylene cetyl ether (25 E.O.)	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
20. Polyoxyethylene ste- aryl ether (20 E.O.)	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70
21. Carboxyvinyl polymer	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
22. Sodium dl-Pyrroli- done carboxylate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23. Disodium edetate	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24. Citric acid	*1	*1	*1	*1	*1	*1	*1	*1	*1
25. Sodium citrate	*1	*1	*1	*1	*1	*1	*1	*1	*1
26. Purified water	*2	*2	*2	*2	*2	*2	*2	*2	*2
Results of the tests	Appearance	*3	no	no	no	no	no	no	no
		*4	⊙	⊙	⊙	⊙	⊙	⊙	⊙
	Color difference ( $\Delta E$ )		3.4	3.0	2.9	2.5	2.8	3.1	2.0
	Evaluation of feeling	*6	⊙	⊙	⊙	⊙	⊙	⊙	⊙
	upon app- lication (*5)	*7	⊙	⊙	⊙	⊙	⊙	⊙	⊙
		*8	⊙	⊙	⊙	⊙	⊙	⊙	⊙

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

\*3: Separation of ultraviolet light absorbent

\*4: Emulsion state (separation)

⊙: good;  $\Delta$ : partly separated; X: separated

\*5: Standard of evaluation:

⊙: good; ○: almost no problem;  $\Delta$ : slight problem;  
X: bad

\*6: rough feel

\*7: sticky feel

\*8: fitness to skin



[illegible]

(contd.)

19. Polyoxyethylene cetyl ether(25 E.O.)	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	
20. Polyoxyethylene ste- aryl ether (20 E.O.)	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70	
21. Carboxyvinyl polymer	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	
22. Soln. of sodium dl- pyrrolidone carboxylate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	
23. Disodium edetate	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	
24. Citric acid	*1	*1	*1	*1	*1	*1	*1	*1	*1	*1	
25, Sodium citrate	*1	*1	*1	*1	*1	*1	*1	*1	*1	*1	
26. Purified water	*2	*2	*2	*2	*2	*2	*2	*2	*2	*2	
Results of the tests	Appearance	*3	-	no	yes	yes	yes	yes	yes	yes	
		*4	△	×	×	×	×	×	×	×	
	Color difference (△E)		9.1	8.5	7.7	7.9	10.3	7.2	8.6	8.1	6.5
	Evaluation of feeling upon app- lication (*5)	*6	○	○	○	×	×	×	×	×	×
		*7	△	×	×	△	△	△	△	×	×
		*8	△	△	×	△	×	△	×	×	△

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

\*3: Separation of ultraviolet light absorbent

\*4: Emulsion state (no separation)

◎ : good; △ : partly separated; X : separated

\*5: Standard of evaluation:

◎ : good; ○ : almost no problem; △ : slight problem; X : bad

\*6: rough feel

\*7: sticky feel

\*8: fitness to skin

[illegible]

(contd.)

21. Carboxyvinyl polymer	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
22. Sodium dl-Pyrroli- done carboxylate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23. Disodium edetate	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24. Citric acid	*1	*1	*1	*1	*1	*1	*1	*1	*1
25. Sodium citrate	*1	*1	*1	*1	*1	*1	*1	*1	*1
26. Purified water	*2	*2	*2	*2	*2	*2	*2	*2	*2
Results of the tests	Appearance	*3	no	no	no	no	no	no	no
		*4	⊙	⊙	⊙	⊙	⊙	⊙	⊙
	Color difference ( $\Delta E$ )		3.2	3.1	3.0	2.3	3.0	2.9	2.5
	Evaluation of feeling upon app- lication (*5)	*6	⊙	⊙	⊙	⊙	⊙	⊙	⊙
		*7	⊙	⊙	⊙	⊙	⊙	⊙	⊙
		*8	⊙	⊙	⊙	⊙	⊙	⊙	⊙

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

\*3: Separation of ultraviolet light absorbent

\*4: Emulsion state (separation)

⊙ : good; △ : partly separated; X: separated

\*5: Standard of evaluation:

⊙ : good; ○ : almost no problem; ⊙ : slight problem;

X : bad

\*6: rough feel

\*7: sticky feel

\*8: fitness to skin

Table 1-4

[illegible]

(contd.)

20. Polyoxyethylene stearyl ether (20 E.O.)			0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70
21. Carboxyvinyl polymer			0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
22. Sodium dl-Pyrrolidone carboxylate			6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23. Disodium edetate			0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24. Citric acid			*1	*1	*1	*1	*1	*1	*1	*1	*1
25. Sodium citrate			*1	*1	*1	*1	*1	*1	*1	*1	*1
26. Purified water			*2	*2	*2	*2	*2	*2	*2	*2	*2
Results of the tests	Appearance	*3	-	no	yes	yes	yes	yes	yes	yes	yes
		*4	△	X	X	X	X	X	X	X	X
	Color difference (△E)		9.1	8.5	7.7	7.9	10.3	7.2	8.6	8.1	6.5
	Evaluation of feeling upon application (*5)	*6	○	○	○	X	X	X	X	X	X
		*7	△	X	X	△	△	△	△	X	X
		*8	△	△	X	△	X	△	X	X	△

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

\*3: Separation of ultraviolet light absorbent

\*4: Emulsion state (no separation)

○ : good; △ : partly separated; X: separated

\*5: Standard of evaluation:

◎ : good; ○ : almost no problem; △ : slight problem; X : bad

\*6: rough feel

\*7: sticky feel

\*8: fitness to skin

[illegible]

(contd.)

22. Sodium dl-Pyrroli- done carboxylate			6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23. Disodium edetate			0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24. Citric acid			*1	*1	*1	*1	*1	*1	*1	*1
25. Sodium citrate			*1	*1	*1	*1	*1	*1	*1	*1
26. Purified water			*2	*2	*2	*2	*2	*2	*2	*2
Results of the tests	Appearance	*3	no	no	no	no	no	no	no	no
		*4	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙
	Color difference (ΔE)		3.0	2.3	2.6	2.2	2.3	2.5	1.9	2.6
	Evaluation of feeling upon app- lication (*5)	*6	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙
		*7	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙
		*8	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

\*3: Separation of ultraviolet light absorbent

\*4: Emulsion state (no separation)

⊙ : good; Δ : partly separated; X: separated

\*5: Standard of evaluation:

⊙ : good; ○ : almost no problem; Δ : slight problem;  
X : bad

\*6: rough feel

\*7: sticky feel

\*8: fitness to skin



[illegible]

(contd.)

22.Sodium dl-Pyrroli- done carboxylate			6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23.Disodium edetate			0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24.Citric acid			*1	*1	*1	*1	*1	*1	*1	*1	*1
25.Sodium citrate			*1	*1	*1	*1	*1	*1	*1	*1	*1
26.Purified water			*2	*2	*2	*2	*2	*2	*2	*2	*2
Results of the tests	Appearance	*3	-	no	yes	yes	yes	yes	yes	yes	yes
		*4	△	×	×	×	×	×	×	×	×
	Color difference (△E)		9.1	8.5	7.7	7.9	10.3	7.2	8.6	8.1	6.5
	Evaluation of feeling upon app- lication (*5)	*6	○	○	○	×	×	×	×	×	×
		*7	△	×	×	△	△	△	△	×	×
		*8	△	△	×	△	×	△	×	×	△

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

\*3: Separation of ultraviolet light absorbent

\*4: Emulsion state (no separation)

◎ : good; △ : partly separated; X: separated

\*5: Standard of evaluation:

◎ : good; ○ : almost no problem; △ : slight problem;  
X : bad

\*6: rough feel

\*7: sticky feel

\*8: fitness to skin

## Experiment 2

Effect of depressing pigmentation of guinea pig induced by UV light

Effect of depressing pigmentation was examined using yellowish brown guinea pigs.

Results of the experiment are tabulated in Table 2.

As can be seen from the results in Table 2, the preparations of the present invention show excellent and lasting pigmentation-depressing effect. Method of experiment:

Back fur of yellowish guinea pigs was clipped off to lay bare the back skin thereof, and the bare back skin was shaved with an electric razor. Each of the shaved backs was covered with a piece of aluminum foil having four square holes ( $2.0 \times 2.0$  cm), and was irradiated with UV-B (having 3 SE lamps;  $140 \text{ mJ/cm}^2$ ) for 90 seconds a day four times every three days. Each of the preparations obtained in Experiment 1 was applied to the irradiated test site from the initiation of the irradiation three times a day for 20 consecutive days (10 consecutive days in the case of Preps 10-17). Concentration of the ingredient in the muscle tissue was measured and pigmentation was scored between 13th day and 20th day or on the 10th and 20th day for Preps 10-17) after initiation of UV light irradiation.

Blackened degree of tested skin was scored with the naked eye according to the following standard.

Scoring standard:

- 3: No pigmentation was observed.
- 2: Slight pigmentation was observed.
- 1: Middle degree pigmentation was observed.
- 0: Pigmentation was observed to the same degree as on control site (non-treated).
- 1: Pigmentation was observed to a stronger degree

than on control site (non-treated).

Results of the experiments:

The preparations of the present invention were confirmed to immediately show excellent pigmentation-depressing effect.

---

Table 2-1

[illegible]

(contd.)

19.Polyoxyethylene cetyl ether(25 E.O.)		1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
20.Polyoxyethylene stearyl ether (20 E.O.)		0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70
21.Carboxyvinyl polymer		0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
22.Soln. of sodium dl-pyrrolidone carboxylate		6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23.Disodium edetate		0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24.Citric acid		*1	*1	*1	*1	*1	*1	*1	*1
25,Sodium citrate		*1	*1	*1	*1	*1	*1	*1	*1
26.Purified water		*2	*2	*2	*2	*2	*2	*2	*2
Scoring of the effect	Concentration of kojic acid in muscle tissue (ug/g)	0.5	0.4	0.4	0.7	0.4	0.6	0.5	0.4
	Degree of pigmentation	3	3	3	3	3	3	3	3
	Days necessary for obtaining pigmentation-curing effect (days)	14	15	13	14	15	13	14	15

\*1: slight amount

\*2: enough amount to make the total amount 100 % by  
weight

• •

[illegible]

(contd.)

19. Polyoxyethylene cetyl ether (25 E.O.)	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
20. Polyoxyethylene stearyl ether (20 E.O.)	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70
21. Carboxyvinyl polymer	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
22. Soln. of sodium dl-pyrrolidone carboxylate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23. Disodium edetate	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24. Citric acid	*1	*1	*1	*1	*1	*1	*1	*1	*1
25. Sodium citrate	*1	*1	*1	*1	*1	*1	*1	*1	*1
26. Purified water	*2	*2	*2	*2	*2	*2	*2	*2	*2
Scoring of the effect	Concentration of kojic acid in muscle tissue ( $\mu\text{g/g}$ )	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
	Degree of pigmentation	1	1	1	1	1	1	1	1
	Days necessary for obtaining pigmentation-curing effect (days)	18	19	18	18	19	19	18	19

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight



Table 2-3 Results of experiments

[illegible]

(contd.)

21. Carboxyvinyl polymer	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
22. Sodium dl-Pyrrolidone carboxylate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
23. Disodium edetate	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24. Citric acid	*1	*1	*1	*1	*1	*1	*1	*1	*1
25. Sodium citrate	*1	*1	*1	*1	*1	*1	*1	*1	*1
26. Purified water	*2	*2	*2	*2	*2	*2	*2	*2	*2
Scoring of the effect	Degree of pigmentation	10th day	0	0	0	0	0	0	0
		20th day	3	3	3	3	3	3	3

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

Table 2-4 Results of experiments

[illegible]

(contd.)

20. Polyoxyethylene ste-	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70	0.70
aryl ether (20 E.O.)									
21. Carboxyvinyl polymer	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
22. Sodium dl-Pyrroli-	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
done carboxylate									
23. Disodium edetate	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
24. Citric acid	*1	*1	*1	*1	*1	*1	*1	*1	*1
25. Sodium citrate	*1	*1	*1	*1	*1	*1	*1	*1	*1
26. Purified water	*2	*2	*2	*2	*2	*2	*2	*2	*2
Scoring of the effect	Degree of pigmen- tation	10th day	0	0	0	0	0	0	0
		20th day	1	1	1	1	1	1	1

\*1: slight amount

\*2: enough amount to make the total amount 100 % by weight

Formulation examples of the present invention are shown b

Formulation example 1 [Cream(1)]

	(% by weight)
1. Kojic acid	1.00
2. Oxybenzonesulfonic acid	0.50
3. Diisopropyl adipate	2.00
4. Isopropyl myristate	3.00
5. Polyoxyethylene cetyl ether (25E.O.)	5.00
6. Stearic acid	5.00
7. Avocado oil	1.00
8. Almond oil	10.00
9. Solution of sodium dl-pyrrolidonecarboxylate	5.00
10. p-Hydroxybenzoic acid ester	0.20
11. Disodium edetate	0.01
12. Purified water to make	100.00

Formulation example 2 [Cream(2)]

	(% by weight)
1. Kojic acid	5.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	0.50
3. Octyldodecyl lactate	1.00
4. Myristyl lactate	0.20
5. Polyoxyethylene lanolin	3.00
6. Dimethylsiloxane methyl (polyoxyethylene-polyoxypropylene copolymer)	3.00
7. Jojoba oil	7.00
8. Decamethylcyclopentasiloxane	3.00
9. Octamethylcyclotetrasiloxane	3.00
10. Dimethylpolysiloxane	5.00
11. Natural vitamin E	0.04
12. 1 % Solution of sodium hyaluronate	2.00
13. Carrageenan	1.00
14. Disodium edetate	0.01
15. Purified water to make	100.00

## Formulation example 3 [Emulsion (1)]

	(% by weight)
1. Kojic acid	4.00
2. 2-Ethylhexyl p-methoxycinnamate	2.00
3. Isostearic acid glyceride	4.00
4. Stearic acid polyoxyethylene monoglyceride	2.00
5. Polyoxyethylene cetyl ether (25E.O.)	0.50
6. Polyoxyethylene oleyl ether (20E.O.)	1.00
7. Stearic acid	0.50
8. Shea butter	0.50
9. Avocado oil	4.00
10. p-Hydroxybenzoic acid ester	0.20
11. Quince seed extract	5.00
12. Xanthan gum	0.14
13. Disodium edetate	0.01
14. Purified water to make	100.00

## Formulation example 4 [Emulsion (2)]

	(% by weight)
1. Kojic acid	0.50
2. Ethylene glycol salicylate	0.10
3. Octyl methoxycinnamate	2.00
4. Coconut oil fatty acid sucrose ester	0.50
5. Myristyl myristate	4.00
6. Coconut oil fatty acid monoethanolamide	2.00
7. Stearic acid	0.50
8. Myristic acid	0.50
9. Avocado oil	4.00
10. Natural vitamin E	0.04
11. p-Hydroxybenzoic acid ester	0.20
12. Sodium hyaluronate	5.00
13. Xanthan gum	0.14
14. Disodium edetate	0.01
15. Purified water to make	100.00

## Formulation example 5 [Lotion]

	(% by weight)
1. Kojic acid glucoside	7.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	2.00
3. 2-Ethylhexyl p-methoxycinnamate	0.05
4. Ethylene glycol monostearate	3.00
5. Polyoxyethylene cetyl ether (60E.O.)	5.00
6. Ginseng extract	2.00
7. Japanese chirate extract	0.50
8. p-hydroxybenzoic acid ester	0.10
10. Sodium citrate	0.30
11. 5 % Solution of elastin hydrolyzate	4.00
12. Disodium edetate	0.01
13. Purified water to make	100.00

## Formulation example 6 [Cream pack]

	(% by weight)
1. Ethyl kojate	2.00
2. 4-tert-butyl-4'-methoxy-dibenzoylmethane	0.50
3. Trimethylolpropane trioctanoate	2.00
4. Oleic acid glyceride	5.00
5. Stearic acid diethanolamide	5.00
6. Stearic acid	5.00
7. Myristic acid	0.50
8. Coconut oil	15.00
9. Natural vitamin E	0.04
10. p-Hydroxybenzoic acid ester	0.20
11. Solution of sodium dl-pyrrolidonecarboxylate	5.00
12. Disodium edetate	0.01
13. Purified water to make	100.00

## Formulation example 7 [Ointment]

	(% by weight)
1. Kojic acid	1.00
2. Oxybenzonesulfonic acid	0.10
3. Phenyl saicylate	0.40

4.	Sodium hydroxymethoxybenzophenonesulfonate	1.00
5.	Sorbitol sesquiisostearate	2.00
6.	Coconut oil fatty acid monoethanolamide	5.00
7.	Vaseline	10.00
8.	Stearic acid	5.00
9.	Oleic acid	1.00
10.	Olive oil	10.00
11.	p-Hydroxybenzoic acid ester	0.20
12.	Carrageenan	5.00
13.	Disodium edetate	0.01
14.	Purified water to make	100.00

## Formulation example 8 [Cataplasm]

	(% by weight)
1. Kojic acid fructoside	0.50
2. Glyceryl p-aminobenzoate	4.00
3. Hexyldecyl dimethyloctanoate	1.00
4. Stearic acid diethanolamide	3.00
5. Polyacrylic acid	27.00
6. Licorice extract (ethanol extract)	0.10
7. Scutellaria root extract (aqueous extract)	0.05
8. Disodium edetate	0.05
9. Sodium polyacrylate	7.00
10. Aluminum chloride	0.30
11. Conc. glycerin	20.00
12. Titanium oxide	4.00
13. Purified water to make	100.00

## Formulation example 9 [Essence]

	(% by weight)
1. Kojic acid	1.00
2. Urocanic acid	0.50
3. 2-Ethylhexyl p-methoxycinnamate	1.00
4. Polyoxyl 40 stearate	0.50
5. Octyldodecyl myristate	1.50
6. Coconut oil fatty acid monoethanolamide	2.00



7.	Stearic acid	0.50
8.	Linolenic acid	0.50
9.	Avocado oil	2.00
10.	Turtle oil	3.00
11.	Natural vitamin E	0.04
12.	p-Hydroxybenzoic acid ester	0.20
13.	1 % Aqueous solution of carboxyvinyl polymer	5.00
14.	Xanthane gum	0.14
15.	Disodium edetate	0.01
16.	Purified water to make	100.00

## Formulation example 10 [Cream(1)]

	(% by weight)
1. Kojic Acid	1.00
2. Oxybenzonesulfonic acid	0.50
3. Phosphatidyl choline	2.00
4. Polyoxyethylene hardened castor oil (OE.O.)	3.00
5. Polyoxyethylene cetyl ether (25E.O.)	5.00
6. Stearic acid	5.00
7. Avocado oil	1.00
8. Almond oil	10.00
Solution of sodium dl-pyrrolidonecarboxylate	5.00
10. p-Hydroxybenzoic acid ester	0.20
11. Disodium edetate	0.01
12. Purified water to make	100.00

## Formulation example 11 [Cream(2)]

	(% by weight)
1. Kojic acid	5.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	0.50
3. Phosphatidyl ethanolamine	1.00
4. Polyoxyethylene castor oil	0.20
5. Plastibase	3.00
6. Polyoxyethylene hydrous lanolin	3.00
7. Jojoba oil	7.00
8. Decamethylcyclopentasiloxane	3.00

9.	Octamethylcyclotetrasiloxane	3.00
10.	Dimethylpolysiloxane	5.00
11.	Natural vitamin E	0.04
12.	1 % Solution of sodium hyaluronate	2.00
13.	Carrageenan	1.00
14.	Disodium edetate	0.01
15.	Purified water to make	100.00

## Formulation example 12 [Emulsion (1)]

	(% by weight)
1. Kojic acid	4.00
2. 2-Ethylhexyl p-methoxycinnamate	2.00
3. Squalane	4.00
4. Ceramide	2.00
5. Polyoxyethylene cetyl ether (25E.O.)	0.50
6. Poxoxyethylene oleyl ether	1.00
7. Stearic acid	0.50
8. Shea butter	0.50
9. Avocado oil	4.00
10. p-Hydroxybenzoic acid ester	0.20
11. Quince seed extract	5.00
12. Xanthane gum	0.14
13. Disodium edetate	0.01
14. Purified water to make	100.00

## Formulation example 13 [Emulsion (2)]

	(% by weight)
1. Kojic acid	0.50
2. Ethylene glycol salicylate	0.10
3. Octyl methoxycinnamate	2.00
4. Poxoxyethylene sorbitol bees was	0.50
5. Light liquid paraffin	4.00
6. Coconut oil fatty acid monoethanolamide	2.00
7. Stearic acid	0.50
8. Myristic acid	0.50
9. Avocado oil	4.00

10.	Natural vitamin E	0.04
11.	p-Hydroxybenzoic acid ester	0.20
12.	Sodium hyaluronate	5.00
13.	Xanthane gum	0.14
14.	Disodium edetate	0.01
15.	Purified water to make	100.00

## Formulation example 14 [Lotion]

	(% by weight)
1. Kojic acid glucoside	7.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	2.00
3. 2-Ethylhexyl p-methoxycinnamate	0.05
4. Lauric polyoxyethylene hardened castor oil (100E.O.)	3.00
5. Polyoxyethylene cetyl ether (60E.O.)	5.00
6. Ginseng extract	2.00
7. Japanese chirate extract	0.50
8. p-hydroxybenzoic acid ester	0.10
9. Ascorbic acid	0.10
10. Sodium citrate	0.30
11. 5 % Solution of elastin hydrolyzate	4.00
12. Disodium edetate	0.01
13. Purified water to make	100.00

## Formulation example 15 [Cream pack]

	(% by weight)
1. Ethyl kojate	2.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	0.50
3. Triisostearic acid polyoxyethylene hardened castor oil (100E.O.)	2.00
4. Phosphatidyl inositol	5.00
5. Stearic acid diethanolamide	5.00
6. Stearic acid	5.00
7. Myristic acid	0.50
8. Coconut oil	15.00
9. Natural vitamin E	0.04
10. p-Hydroxybenzoic acid ester	0.20

11.	Solution of sodium dl-pyrrolidonecarboxylate	5.00
12.	Disodium edetate	0.01
13.	Purified water to make	100.00

## Formulation example 16 [Ointment]

	(% by weight)
1. Kojic acid	1.00
2. Oxybenzonesulfonic acid	0.10
3. Phenyl salicylate	0.40
4. Sodium hydroxymethoxybenzophenonesulfonate	1.00
5. Plastibase	2.00
6. Coconut oil fatty acid monoethanolamide	5.00
7. Vaseline	10.00
8. Stearic acid	5.00
9. Oleic acid	1.00
10. Olive oil	10.00
11. p-Hydroxybenzoic acid ester	0.20
12. Carrageenan	5.00
13. Disodium edetate	0.01
14. Purified water to make	100.00

## Formulation example 17 [Cataplast]

	(% by weight)
1. Kojic acid fructoside	0.50
2. Glyceryl p-aminobenzoate	4.00
3. Isostearic acid polyoxyethylene hardened castor oil	1.00
4. Stearic acid diethanolamide	3.00
5. Polyacrylic acid	27.00
6. Licorice extract (ethanol extract)	0.10
7. Scutellaria root extract (aqueous extract)	0.05
8. Disodium edetate	0.05
9. Sodium polyacrylate	7.00
10. Aluminum chloride	0.30
11. Conc. glycerin	20.00
12. Titanium oxide	4.00
13. Purified water to make	100.00

## Formulation example 18 [Essence]

	(% by weight)
1. Kojic acid	1.00
2. Urocanic acid	0.50
3. 2-Ethylhexyl p-methoxycinnamate	1.00
4. Liquid isopraffin	0.50
5. Dipalmitoyl phosphatidyl choline	1.50
6. Coconut oil fatty acid monoethanolamide	2.00
7. Stearic acid	0.50
8. Linolenic acid	0.50
9. Avocado oil	2.00
10. Turtle oil	3.00
11. Natural vitamine E	0.04
12. p-Hydroxybenzoic acid ester	0.20
13. 1 % Aqueous solution of carboxyvinyl polymer	5.00
14. Xanthan gum	0.14
15. Disodium edetate	0.01
16. Purified water to make	100.00

## Formulation example 19 [Cream(1)]

	(% by weight)
1. Kojic acid	1.00
2. Hydroxybenzenesulfonic acid	0.50
3. Mannitol	2.00
4. Polyethylene glycol 400	3.00
5. Polyoxyethylene cetyl ether (25E.O.)	5.00
6. Stearic acid	5.00
7. Avocado oil	1.00
8. Almond oil	10.00
9. Solution of sodium dl-pyrrolidonecarboxylate	5.00
10. p-Hydroxybenzoic acid ester	0.20
11. Disodium edetate	0.01
12. Purified water to make	100.00

## Formulation example 20 [Cream(2)]

	(% by weight)
1. Kojic acid	5.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	0.50
3. Jojoba alcohol	1.00
4. Sorbitol	3.00
5. Epicatechin gallate	0.50
6. Dimethylsiloxane-methyl(polyoxyethylene-polyoxypropylene copolymer)	3.00
7. jojoba oil	7.00
8. Decamethylcyclopentasiloxane	3.00
9. Octamethylcyclotetrasiloxane	3.00
10. Dimethylpolysiloxane	5.00
11. Natural vitamin E	0.04
12. 1 % Solution of sodium hyaluronate	2.00
13. Carrageenan	1.00
14. Disodium edetate	0.01
15. Purified water to make	100.00

## Formulation example 21 [Emulsion (1)]

	(% by weight)
1. Kojic acid	4.00
2. 2-Ethylhexyl p-methoxycinnamate	2.00
3. Polyethylene glycol 4000	3.00
4. Octyl dodecanol	3.00
5. Polyoxyethylene cetyl ether (25E.O.)	0.50
6. Polyoxyethylene oleyl ether (20E.O.)	1.00
7. Stearic acid	0.50
8. Shea butter	0.50
9. Avocado oil	4.00
10. p-Hydroxybenzoic acid ester	0.20
11. Quince seed extract	5.00
12. Xanthane gum	0.14
13. Disodium edetate	0.01
14. Purified water to make	100.00

## Formulation example 22 [Emulsion (2)]

	(% by weight)
1. Kojic acid	0.50
2. Ethylene glycol salicylate	0.10
3. Octyl methoxycinnamate	2.00
4. Batyl alcohol	3.50
5. Shikimic acid	2.00
6. Coconut oil fatty acid monoethanolamide	2.00
7. Stearic acid	0.50
8. Myristic acid	0.50
9. Avocado oil	4.00
10. Natural vitamin E	0.04
11. p-Hydroxybenzoic acid ester	0.20
12. Sodium hyaluronate	5.00
13. Xanthane gum	0.14
14. Disodium edetate	0.01
15. Purified water to make	100.00

## Formulation example 23 [Lotion]

	(% by weight)
1. Kojic acid glucoside	7.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	2.00
3. 2-Ethylhexyl p-methoxycinnamate	0.05
4. Ethylene glycol ethyl ether	3.00
5. Polyoxyethylene cetyl ether (60E.O.)	5.00
6. Ginseng extract	2.00
7. Japanese chirate extract	0.50
8. p-hydroxybenzoic acid ester	0.10
9. Ascorbic acid	0.10
10. Sodium citrate	0.30
11. 5 % Solution of elastin hydrolyzate	4.00
12. Disodium edetate	0.01
13. Purified water to make	100.00

## Formulation example 24 [Cream pack]

	(% by weight)
1. Ethyl kojate	2.00
2. 4-tert-Butyl-4'-methoxy-dibenzoylmethane	0.50
3. Decyltetradecanol	2.00
4. Polyethylene glycol 1500	5.00
5. Stearic acid diethanolamide	5.00
6. Stearic acid	5.00
7. Myristic acid	0.50
8. Coconut oil	15.00
9. Natural vitamin E	0.04
10. p-Hydroxybenzoic acid ester	0.20
11. Solution of sodium dl pyrrolidonecarboxylate	5.00
12. Disodium edetate	0.01
13. Purified water to make	100.00

## Formulation example 25 [Ointment]

	(% by weight)
1. Kojic acid	1.00
2. Hydroxybenzenesulfonic acid	0.10
3. Phenyl salicylate	0.40
4. Sodium hydroxymethoxybenzophenonesulfonate	1.00
5. Isoamyl octyl gallate	2.00
6. Coconut oil fatty acid monoethanolamide	5.00
7. Vaseline	10.00
8. Stearic acid	5.00
9. Oleic acid	1.00
10. Olive oil	10.00
11. p-Hydroxybenzoic acid ester	0.20
12. Carrageenan	5.00
13. Disodium edetate	0.01
14. Purified water to make	100.00

## Formulation example 26 [Cataplasm]

	(% by weight)
1. Kojic acid fructoside	0.50



2.	Glyceryl p-aminobenzoate	4.00
3.	Rutin	1.00
4.	Stearic acid diethanolamide	3.00
5.	Polyacrylic acid	27.00
6.	Licorice extract (ethanol extract)	0.10
7.	Scutellaria root extract (aqueous extract)	0.05
8.	Disodium edetate	0.05
9.	Sodium polyacrylate	7.00
10.	Aluminum chloride	0.30
11.	Conc. glycerin	20.00
12.	Titanium oxide	4.00
13.	Purified water to make	100.00

## Formulation example 27 [Essence]

	(% by weight)
1. Kojic acid	1.00
2. Urocanic acid	0.50
3. 2-Ethylhexyl p-methoxycinnamate	1.00
4. Isopropanol	0.50
5. Benzyl alcohol	0.05
6. Xylose	1.50
7. Coconut oil fatty acid monoethanolamide	2.00
8. Stearic acid	0.50
9. Linolenic acid	0.50
10. Avocado oil	2.00
11. Turtle oil	3.00
12. Natural vitamine E	0.04
13. p-Hydroxybenzoic acid ester	0.20
14. 1 % Aqueous solution of carboxyvinyl polymer	5.00
15. Xanthane gum	0.14
16. Disodium edetate	0.01
17. Purified water to make	100.00

It has been confirmed that the above-described Formulation Examples 1 to 27 provide preparations having the same satisfactory results as are shown in Tables 1 and 2.

Claims

1. A preparation for epidermis containing kojic acid and/or its derivative and an ultraviolet light absorbent, which further contains at least one member selected from the group consisting of fatty acid esters and fatty acid glycerides; hydrocarbons, lipids and hardened or non-hardened fats; and oils, alcohols and polyphenols.
2. The preparation for epidermis according to claim 1, wherein said alcohols are those selected from the group consisting of lower alcohols, higher alcohols, sugar alcohols, polyhydric alcohols and polyhydric alcohol alkyl ethers, and said polyphenols are those selected from the group consisting of catechin, esters of gallic acid, flavone and tannin.
3. The preparation for epidermis according to claim 1, wherein said hydrocarbons are those selected from the group consisting of paraffinic hydrocarbons and olefinic hydrocarbons, said lipids are those selected from the group consisting of glycerophospholipids, sphingophospholipids and sphingoglycolipids, and said hardened or non-hardened fats and oils are those selected from the group consisting of polyoxyethylene hardened fats and oils and polyoxyethylene non-hardened fats and oils.
4. The preparation for epidermis according to claim 1, wherein said fatty acid esters are those selected from the group consisting of higher fatty acid esters, ethylene glycol fatty acid esters, polyethylene glycol fatty acid esters, propylene glycol fatty acid esters, glycol fatty acid esters, trimethylolpropane fatty acid esters, pentaerythritol fatty acid esters, sorbitol fatty acid esters, polyoxyethylene fatty acid esters and sugar fatty acid esters and said fatty acid glycerides are those selected from the group consisting of

glycerin fatty acid esters, polyglycerin fatty acid esters and polyoxyethyleneglycerin fatty acid esters.

5. The preparation for epidermis according to claim 1, wherein said alcohol is octyldodecanol.

6. The preparation for epidermis according to claim 1, wherein said alcohol is polyethylene glycol.

7. The preparation for epidermis as described in claim 1, wherein said polyphenol is epigallocatechin.

8. The preparation for epidermis according to claim 1, wherein said polyphenol is shikimic acid.

9. The preparation for epidermis as described in any of claims 1 to 8, wherein said kojic acid derivative is kojic acid glycoside.

10. The preparation for epidermis according to claim 9, wherein said kojic acid glycoside is kojic acid glucoside.

11. The preparation for epidermis according to claim 9, wherein said kojic acid glycoside is kojic acid fructoside.

12. The preparation for epidermis according to any of claims 1 to 8, wherein said kojic acid derivative is ethyl kojate.

13. The preparation for epidermis according to any of claims 1 to 12, wherein said one member is incorporated in an amount of 0.001 to 20 % by weight based on the total amount of the preparation.

14. The preparation for epidermis according to claim 13, wherein said one member is incorporated in an amount of 0.1 to

10 % by weight based on the total amount of the preparation.

15. The preparation for epidermis according to any of claims 1 to 14, which is in a form selected from the group consisting of cataplasma, plaster, paste, cream, ointment, aerosol, emulsion, lotion, essence, pack, gel, powder, foundation, suncare and bath salts.

---

Patents Act 1977 Examiner's report to the Comptroller under Section 17 (The Search report)		Application number GB 9411992.2
Relevant Technical Fields		Search Examiner C Sherrington
(i) UK Cl (Ed.M)     A5B (BFE, BFH, BJB) (ii) Int Cl (Ed.5)     A61K 7/40, 7/42, 31/35, 47/00, 7/48		Date of completion of Search 19 September 1994
Databases (see below) (i) UK Patent Office collections of GB, EP, WO and US patent specifications. (ii) ONLINE DATABASES : WPI, CLAIMS, DIALOG/PHARM		Documents considered relevant following a search in respect of Claims :- 1-15

Categories of documents

X: Document indicating lack of novelty or of inventive step.	P: Document published on or after the declared priority date but before the filing date of the present application.
Y: Document indicating lack of inventive step if combined with one or more other documents of the same category.	E: Patent document published on or after, but with priority date earlier than, the filing date of the present application.
A: Document indicating technological background and/or state of the art.	&: Member of the same patent family; corresponding document

Category	Identity of document and relevant passages		Relevant to claim(s)
X	US 4985455	(SANSHO SEIYAKA CO LTD) whole document	1-4, 14,15 (at least)
A	JP 020200622 A	(SANSHO PHARM KK) Derwent WPI Abstract Accession No 90-286007/38	1
X	JP 050078383 A	(SANSHO PHARM CO LTD) Derwent WPI Abstract Accession No 93-146250/18	1.4, 8-11, 13-15 (at least)
P,X	JP 060048935 A	(SANSHO PHARM CO LTD) Derwent WPI Abstract Accession No 94-097774/12	1,2,5, 6,15 (at least)

Databases: The UK Patent Office database comprises classified collections of GB, EP, WO and US patent specifications as outlined periodically in the Official Journal (Patents). The on-line databases considered for search are also listed periodically in the Official Journal (Patents).

**THIS PAGE BLANK (USPTO)**

---